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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,285	03/02/2005	Nitin Bhalachandra Dharmadhikari	006420.00004	4683

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EXAMINER	
SIMMONS, CHRIS E	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,285	DHARMADHIKARI ET AL.	
	Examiner	Art Unit	
	CHRIS E. SIMMONS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,10,11,14-18,23 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,10,11,14-18,23 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/2008, 02/26/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Newly submitted claim 30 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the invention of claim 30 and the invention originally claimed are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the originally claimed product can be used intravenously as a muscle relaxant.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 30 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Rejoinder Reminder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise

require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112 (New Matter)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, 10, 11, 14-18, 23 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent claims 1 and 31 recite the new limitation, "a *greater* rate and extent of absorption". *Emphasis added.* However, the Examiner does not readily see support in the application as originally filed for a *greater* rate and extent of absorption. It appears that previous recitations to the rate and extent of absorption was modified by the term "enhanced" instead of "greater" or "increased". The examiner does not find these terms synonymous as explained in the Office action mailed submitted on 06/26/2008 (see paragraph bridging pages 6 and 7).

Claim Rejections - 35 USC § 112 - Indefinite

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 10, 11, 15-18, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the limitation "not more than about." The term "not more than" delineates only numerical values not more than the recited value where the term "about" may be less than or more than the recited value. Because of the conflict of terms, it is unclear which term is limiting. See also MPEP 2173.05(b) (citing Amgen v. Chugai, 18 USPQ2d 1016 (Fed. Cir. 1991), in which the phrase "at least about" was held indefinite).

Claim Rejections - 35 USC § 103

The two rejections will be discussed together infra, considering the issues for both are essentially the same.

Claims 1, 7, 10, 11, 14-18, 23 and 31 were rejected under 35 U.S.C. 103(a) as being unpatentable over Liversidge et al. (USP 5,145,684) in view of Scaife et al. (USP 6,407,128). **This rejection is maintained.**

Claims 1, 7, 10, 11, 14-18, 23 and 31 were rejected under 35 U.S.C. 103(a) as being unpatentable over Martin et al (USP 4,344,934) in view of Scaife et al (USP 6,407,128). **This rejection is maintained.**

Applicant asserts that the examiner erred in the Final Office action submitted 06/26/2008 in interpreting the meaning of "reasonable expectation of success" by stating that "some predictability" in practicing the claimed method is enough to satisfy the reasonable predictability required by the MPEP. Applicant's assertion is not

persuasive because the MPEP is clear that some predictability is sufficient to be reasonably predictable. Examiner also notes that later in applicant's response at page 10, last sentence of second paragraph; applicant recites the MPEP: "Obviousness does not require absolute predictability, however, *at least some degree of predictability is required*. See MPEP 2143.02". *Emphasis in original.* Accordingly, examiner's interpretation is consistent with MPEP requirements because there is, at least, some predictability in accomplishing the claimed method successfully. Applicant's discussion on probability is unpersuasive because currently the examiner's rejections are not based on probability.

Applicant presents several arguments that the prior art does not result in an increase in ***both*** rate of absorption and extent of absorption. However, applicant appears to have already acknowledged that bioavailability is considered to represent ***both*** rate and extent of absorption. The examiner refers to [0021] in the instant specification: "Bioavailability referred to herein is rate ***and*** extent to which the active drug ingredient, metaxalone, is absorbed into the systemic circulation from the pharmaceutical composition of the present invention"; thus, bioavailability in the cited references is considered to reasonably refer to ***both*** rate and extent of absorption. Furthermore, the secondary reference is directed to a method of increasing the bioavailability of metaxalone (abstract) and explicitly teaches "the subject of this invention is the unexpected finding that administration of metaxalone with food increases both the rate and extent of absorption via the oral dosage form in human

subjects" (col. 2 , ll. 6-9). Accordingly, this disclosure is considered to provide more evidence that the cited prior art referrers to both extent and rate of absorption.

Applicant's arguments concerning whether the secondary reference shows data that resulted in both rate and extent of absorption are considered not persuasive in terms of addressing the merits of the instant case. The claimed subject matter is based on the comparison of pharmacokinetic properties between applicant's composition and the already known composition, Skelexin®, when each are taken on an empty stomach, particularly, that the claimed composition, when taken on an empty stomach, produces a greater rate and extent of absorption when taken on an empty stomach, as compared to skelaxin®. At issue, is whether the claimed composition would be obvious over the cited references. Applicant arguments that focus on the Tmax and other pharmacokinetic properties in the secondary reference alleging it shows that the reference did not result in an increase in both rate and extent of absorption would appear to be irrelevant because this pharmacokinetic data in Table IIb at col. 5 of the reference is a comparison of Skelaxin® when taken with and without food. The instant claims do not read on a comparison of compositions with and without food. It is a comparison of compositions where both are taken without food. Accordingly, it is unclear what the relevance of Tmax and AUC in Table IIb is regarding the merits of the instant claims.

Applicant alleges that the examiner has not enumerated any reason or facts to support the contention that there is a predictability in achieving the result, i.e., that both the rate and extent of absorption would be increased. Applicant further argues that there

is no motivation or suggestion to use metaxalone as disclosed in the primary references. These allegations are unpersuasive. The primary reference discloses ways to increase the bioavailability (i.e., rate and extent of absorption) of a wide variety of active agents that would be expected to benefit from increased solubility and bioavailability. The secondary reference is directed to increasing the bioavailability (i.e., rate and extent of absorption) of the hydrophobic compound, metaxalone; suggesting some benefit from increasing these properties. One would reasonably expect to increase the bioavailability of Skelaxin® by using it in the methods described in the primary references for increasing bioavailability. A reasonable expectation is adequate for a *prima facie* case of obviousness.

As stated above, applicant's arguments against the Tmax and other pharmacokinetic properties in Table IIb are not persuasive because they would appear to be focusing on a comparison between metaxalone taken with food as compared to without food instead of what is currently claimed, i.e., a metaxalone composition comprising at least 99% of the metaxalone having a particle size of not more than about 10 microns to Skelaxin®. Purely in arguendo, assuming there is some relevance in arguing the differences of the disclosed Tmax and AUC of the secondary reference regarding the merits of the instant claims, the examiner would still maintain the position that an increase or decrease of Tmax does not inherently mean the absorption will increase or decrease, respectively, because Tmax also relies on excretion. The examiner appreciates the reference provided by the applicant as support that Tmax is closely related to absorption, however, these references, at best, provide support only

that Tmax is closely related to absorption. As support, the examiner cites, Journal of the American Pharmaceutical Association (2001): 41(6):856-867, stating, at page 4 0f 11, "the use of Tmax as a measure of absorption rate has been debated. ***Mathematically***, Tmax is a function of both absorption and elimination rate constants. It is highly dependent on the sampling scheme, and it is therefore difficult to use it to detect differences between two products, especially when tmax values are less than 2 hours. In contrast, for slow-releasing dosage forms, plasma concentrations are maintained at a plateau for a long time and tmax does not reflect the rate of bioavailability. Although the absorption rate constant (ka) is a parameter for assessing the rate of absorption, it is highly dependent on the pharmacokinetic model used to derive the parameter." Based on limitations associated with using Cmax and tmax as measures of rate of absorption, some authors have recommended using other methods as alternative measures (see page 4 of 11).

At page 13 of the instant response, applicant seems to be arguing that secondary considerations have been put forth but have been ignored. Applicant claims that other artisans have "worked to make Skelaxin® more bioavailability but did not reach the achievements made by the present invention". This is not a proper showing of evidence for secondary considerations such as long-felt need and failure of others. This argument is unpersuasive because the applicant must present clear and convincing evidence that others have *tried but failed* according to guidelines set forth in the MPEP 716.04 R2. The examiner does not readily recognize where applicant has properly demonstrated

the "failure of others" to increase the bioavailability of metaxalone. Accordingly, the argument is unpersuasive.

Applicant argues that there was no reasonable expectation of successfully increasing bioavailability of Skelaxin® on an empty stomach. However, the primary reference discloses ways to increase the bioavailability (i.e., rate and extent of absorption) of a wide variety of active agents that would be expected to benefit from increased solubility and bioavailability. The secondary reference is directed to increasing the bioavailability (i.e., rate and extent of absorption) of the hydrophobic compound, metaxalone; suggesting some benefit from increasing these properties. One would reasonably expect to increase the bioavailability of Skelaxin® by using it in the methods described in the primary references for increasing bioavailability. A reasonable expectation is adequate for a *prima facie* case of obviousness.

Applicant alleges that no reason was provided for why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed. Examiner disagrees and refers applicant to the prior Office action submitted 06/26/2008 and supra.

At page 14, applicant claims unexpected results, i.e., the increase in bioavailability of metaxalone as compared to Skelaxin® on an empty stomach. Applicant alleges the result is unexpected, particularly in view of the "fact that the only previous solution to the problem was recited in the secondary reference, which solution produced a contrary result (decreased rate of absorption). Applicant alleges the examiner's error "is the result of considering prior art selectively rather than as a whole." Examiner

disagrees. As outlined above, applicant seems to be confusing what is being compared in the reference and what is being compared in the instant claims. The secondary reference compares, at Table IIb at col. 5, the AUC, Cmax and Tmax of the *same* composition given to people *with food and without* food. The instant claims are directed to a comparison of properties of 2 *different* compositions when taken on an empty stomach. The fact that Skelaxin® has differing pharmacokinetics when taken on an empty stomach as compared to when taken on a full stomach or with food is of not pertinent to the matter at hand with regard to what is instantly claimed. The combination of the primary references with the secondary reference provides one with a reasonable expectation of successfully increasing bioavailability of metaxalone on an empty stomach (or when taken with food).

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRIS E. SIMMONS whose telephone number is (571)272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. E. S./
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612